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Mayes 09/813,093 Page 1

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FILE COVERS 1907 - 1 Jul 2003 VOL 139 ISS 1 FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d stat que
L1 21631 SEA FILE=REGISTRY ABB=ON HEXANEDIOL/BI
L2 10611 SEA FILE=REGISTRY ABB=ON PENTANEDIOL/BI
L3 2059 SEA FILE=REGISTRY ABB=ON HEPTANEDIOL/BI
L4 29042 SEA FILE=HCAPLUS ABB=ON L1 OR HEXANEDIOL?
L5 20324 SEA FILE=HCAPLUS ABB=ON L2 OR PENTANEDIOL?
L6 2693 SEA FILE=HCAPLUS ABB=ON L3 OR HEPTANEDIOL?
L8 1 SEA FILE=HCAPLUS ABB=ON PURIFICATION+ALL/CV (L) (PEPTIDE? OR PROTEIN?) AND (L4 OR L5 OR L6)

=> d ibib abs hitrn 18

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1999:717837 HCAPLUS

DOCUMENT NUMBER:

131:314241

TITLE:

Stabilized protein crystals, formulations containing

them and methods of making them

INVENTOR(S):

Margolin, Alexey L.; Khalaf, Nazer K.; St. Clair, Nancy L.; Rakestraw, Scott L.; Shenoy, Bhami C.

PATENT ASSIGNEE(S):

Altus Biologics Inc., USA PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

SOURCE:

· 1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND		DATE			A.	PPLI	CATI	ои ис	Э.	DATE				
WO 9955310				A1 19991104				M(0 19	99-U	9	19990427						
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		DE,	DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	ΙL,	ΙN,	IS,	
														LV,				
		MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	

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TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2330476
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                             19991104
                                            CA 1999-2330476
                                                             19990427
     AU 9937646
                       Α1
                             19991116
                                            AU 1999-37646
                                                              19990427
     AU 757991
                             20030313
                       В2
                             20010207
                                            EP 1999-920064
     EP 1073421
                       Α1
                                                              19990427
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     JP 2002512949
                       T2
                             20020508
                                            JP 2000-545510
                                                              19990427
     US 2002045582
                       Α1
                             20020418
                                            US 1999-374132
                                                              19990810
     US 6541606
                       В2
                             20030401
                                         US 1998-83148P
PRIORITY APPLN. INFO.:
                                                          P 19980427
                                         US 1998-224475
                                                          A2 19981231
                                         US 1997-70274P
                                                          P 19971231
                                         WO 1999-US9099
                                                          W 19990427
AB
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Methods are provided for the stabilization, storage, and delivery of biol. active macromols., such as proteins, peptides and nucleic acids. Methods are provided for the crystn. of proteins and nucleic acids and for the prepn. of stabilized protein or nucleic acid crystals for use in dry or slurry formulations in pharmaceutical and veterinary formulations, diagnostics, cosmetics, food, and agricultural feeds. The crystals are stabilized by addn. of excipients such as carbohydrates or by encapsulating them in a polymeric carrier. Methods are presented for encapsulating proteins, glycoproteins, enzymes, antibodies, hormones, and peptide crystals or crystal formulations into compns. for biol. delivery to humans and animals. Thus, lipase from Candida rugosa was dissolved in distd. water, treated with celite, adjusted to pH 4.8 with AcOH, filtered, ultrafiltered to remove proteins of <30 kDa mol. wt., and crystn. was initiated by addn. of 2-methyl-2,4-pentanediol. Sucrose was added to the mother liquor to a concn. of 10%, and the crystals were sepd. by centrifugation, suspended in EtOH, and air dried at room temp. Alternatively, the lipase crystals were crosslinked and encapsulated in lactic acid/glycolic acid copolymer; the microspheres formed were 90 .mu.m in diam.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d stat que
          21631 SEA FILE=REGISTRY ABB=ON HEXANEDIOL/BI
L1
          10611 SEA FILE=REGISTRY ABB=ON PENTANEDIOL/BI
L2
           2059 SEA FILE=REGISTRY ABB=ON HEPTANEDIOL/BI
L3
          29042 SEA FILE=HCAPLUS ABB=ON L1 OR HEXANEDIOL?
L4
                                         L2 OR PENTANEDIOL?
          20324 SEA FILE=HCAPLUS ABB=ON
L5
           2693 SEA FILE=HCAPLUS ABB=ON
                                         L3 OR HEPTANEDIOL?
L6
            712 SEA FILE=HCAPLUS ABB=ON
                                         (PURIF? OR SEPARAT? OR ISOLAT?) AND
L9
                CHROMATO? AND (L4 OR L5 OR L6)
             97 SEA FILE=HCAPLUS ABB=ON
                                         L9(L)ELUT?
L10
             20 SEA FILE=HCAPLUS ABB=ON
                                         L10 AND MOLECULE?
L11
              3 SEA FILE=HCAPLUS ABB=ON
                                         L11 AND BUFFER?
L12
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=> d ibib abs hitrn 112 1-3

L12 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2002:736273 HCAPLUS

DOCUMENT NUMBER: 137:259637 Method for purification of molecules TITLE: using unbranched terminal alkyldiols INVENTOR(S): Hauser, Terry Allen; Hayenga, Kirk James PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.

PCT Int. Appl., 53 pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 2002074791 A1 20020926 WO 2002-EP3021 20020314. W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002183483 A1 20021205 US 2001-813093 20010319 US 2001-813093 A 20010319 PRIORITY APPLN. INFO.: The current invention provides methods for mol. purifn . by RP-LC and RP-HPLC that uses unbranched terminal alkyldiols as eluting solvents. In particular, the present invention purifies mols., particularly proteins and peptides, on reverse phase liq. chromatog. columns using a buffer contg. either 1,5-pentanediol, 1,6-hexanediol or 1,7heptanediol. Growth hormone antagonist and five other peptides with purified on an Amberchrom CG71-M column eluted with a linear gradient of 1,6-hexanediol in Tris HCl, pH 7.5. 111-29-5, 1,5-Pentanediol 629-11-8, 1,6-Hexanediol 629-30-1, 1,7-Heptanediol

IT

RL: NUU (Other use, unclassified); USES (Uses)

(method for purifn. of mols. using unbranched terminal

alkyldiols as eluting solvents)

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 4 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:537520 HCAPLUS

DOCUMENT NUMBER: 135:134285

Purification of polypeptides by TITLE:

> reversed-phase liquid chromatography Fahrner, Robert Lee; Reifsnyder, David

INVENTOR(S): Genentech, Inc., USA PATENT ASSIGNEE(S):

U.S., 27 pp. SOURCE: CODEN: USXXAM

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. _____ ______ US 6265542 ... B1 20010724 US 1998-168548 19981008

no had

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PRIORITY APPLN. INFO.:
                                        US 1997-63119P
                                                          P 19971024
    A process for purifying polypeptide mols. from contaminants is
     provided. In this process a mixt. contq. the mol. (peptide,
     polypeptide, or biol. active non-peptidyl compd.) and its contaminants is
     loaded onto a reversed-phase liq. chromatog. column and the
     mol. is eluted from the column with a buffer
     contq. hexylene glycol. Lysozyme was sepd. from ovalbumin,
     substance P was sepd. from bradykinin, and hydrocortisone was
     sepd. from progesterone by reversed-phase lig. chromatog
     . using hexylene glycol.
     126-30-7, Neopentyl glycol
     RL: PRP (Properties)
        (as solvent in IGF-I purifn. from mutant; purifn.
        of polypeptides by reversed-phase liq. chromatog.)
     107-41-5, Hexylene glycol
     RL: NUU (Other use, unclassified); USES (Uses)
        (purifn. of polypeptides by reversed-phase liq.
        chromatog.)
                               THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         65
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L12 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
                         1999:297447 HCAPLUS
DOCUMENT NUMBER:
                         130:293612
                         Purification of proteins and other
TITLE:
                         molecules using reversed-phase liq.
                         chromatog. and elution using
                         hexylene glycol.
INVENTOR(S):
                         Fahrner, Robert L.; Reifsnyder, David
PATENT ASSIGNEE(S):
                         Genentech, Inc., USA
                         PCT Int. Appl., 47 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     DATENT NO
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                                           ADDITCATION NO
                                                             DATE
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	PATENT NO. KIND DATE								APPLICATION NO. DATE									
WO 9921889					A1 19990506					WO 1998-US21238 19981008								
		W:	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
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	CA 2306447				A1 19990517				CA 1998-2306447 19981008									
	AU 9910725							A	U 19	99-1		19981008						
AU 740665			B2 20011108															
,	EP 1025126						EP 1998-953320 19981008											
				B1 20030416				FR, GB, GR, IT, LI, LU										
					CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
•														_	10001000			
JP 2001521044				T2 2001		1106		JP 2000-517996					1998.	31008				
AT 237636				E 200			0515		*					19981008				
ZA 9809424				A 20000417				ZA 1998-9424 US 1997-957760 A						19981015				
PRIO	RIT	APP	LN.	INFO	.:				į	US 1	997-	9577	60	A	1997	1024		

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WO 1998-US21238 W 19981008
AΒ
     This invention provides a process for purifying a mol.
     selected from the group consisting of peptides, proteins and biol. active
     non-peptidyl compds. The method consists of loading a mixt. contq. the
     mol. onto a reversed-phase liq. chromatog. column and
     eluting the mol. from the column with a buffer
     contg. the non-flammable eluent hexylene glycol.
                                                       The process is
     illustrated using insulin-like growth factor I.
     107-41-5, Hexylene glycol
     RL: BUU (Biological use, unclassified); NUU (Other use, unclassified);
     BIOL (Biological study); USES (Uses)
        (purifn. of proteins and other mols. using reversed-phase
        liq. chromatog. and elution using hexylene glycol.)
REFERENCE COUNT:
                         3
                               THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> d stat que
          21631 SEA FILE=REGISTRY ABB=ON HEXANEDIOL/BI
L2
          10611 SEA FILE=REGISTRY ABB=ON PENTANEDIOL/BI
L3
           2059 SEA FILE=REGISTRY ABB=ON HEPTANEDIOL/BI
          29042 SEA FILE=HCAPLUS ABB=ON L1 OR HEXANEDIOL?
L4
L5
          20324 SEA FILE=HCAPLUS ABB=ON L2 OR PENTANEDIOL?
           2693 SEA FILE=HCAPLUS ABB=ON L3 OR HEPTANEDIOL?
L6
              1 SEA FILE-HCAPLUS ABB-ON PURIFICATION+ALL/CV (L) (PEPTIDE? OR
L8
                PROTEIN?) AND (L4 OR L5 OR L6)
            712 SEA FILE=HCAPLUS ABB=ON
                                         (PURIF? OR SEPARAT? OR ISOLAT?) AND
                CHROMATO? AND (L4 OR L5 OR L6)
L10
             97 SEA FILE=HCAPLUS ABB=ON L9(L)ELUT?
             20 SEA FILE=HCAPLUS ABB=ON L10 AND MOLECULE?
L11
L12
              3 SEA FILE=HCAPLUS ABB=ON L11 AND BUFFER?
L13
              2 SEA FILE=HCAPLUS ABB=ON
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                CHROMAT? AND ALKYLDIOL? (L) (ELUT? OR BUFFER?)
L14
              1 SEA FILE=HCAPLUS ABB=ON L13 NOT (L12 OR L8)
=> d ibib abs hitrn 114
L14 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
                         1999:640094 HCAPLUS
DOCUMENT NUMBER:
                         131:331689
                         Determination of 4-demethoxy-3'-deamino-3'-aziridinyl-
TITLE:
                         4'-methylsulphonyldaunorubicin and its 13-hydroxy
                         metabolite by direct injection of human plasma into a
                         column-switching liquid chromatography
                         system with mass spectrometric detection
                         Breda, M.; Basileo, G.; Fonte, G.; Long, J.; James, C.
AUTHOR (S):
                         Drug Metabolism Research, Pharmacia and Upjohn, Milan,
CORPORATE SOURCE:
                         20014, Italy
                         Journal of Chromatography, A (1999), 854(1 + 2), 81-92
SOURCE:
                         CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER:
                         Elsevier Science B.V.
DOCUMENT TYPE:
                         Journal
                         English
LANGUAGE:
    A selective, sensitive, and fully automated column-switching HPLC system
    using direct injection of human blood plasma followed by MS detection was
    developed to det. the concns. of 4-demethoxy-3'-deamino-3'-aziridinyl-4'-
    methylsulfonyldaunorubicin (PNU-159548) and its 13-hydroxy metabolite
```

(PNU-169884). A 50-.mu.L human plasma sample was directly introduced into a C4-alkyldiol silica clean-up column sepg. analytes from proteins and polar endogenous compds. using water and methanol as the mobile phase. The fraction contg. PNU-159548 and its metabolite was back-flushed and transferred onto the anal. column. The compds. were sepd. on a Zorbax SB C8 column (150.times.4.6 mm, 5 .mu.m) under gradient elution conditions with the mobile phase of acetonitrile and 2 mM ammonium formate pH 3.5. The MS detection was by atm. pressure ionization with multiple reaction monitoring in pos. ion mode. Linearity was demonstrated over the calibration range of 0.051-10.291 ng/mL for PNU-159548 and 0.104-10.434 ng/mL for PNU-169884. The assay was validated with respect to accuracy, precision, and analyte stability. The method is suitable for use in Phase I clin. studies. REFERENCE COUNT: THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT